REMARKS

Claims 1 to 42, as amended, appear in this application for the Examiner's review and consideration. Claims 27 to 42 are withdrawn from consideration, as being drawn to a non-elected invention. The amendments to the claims are fully supported by the specification and claims as originally filed. Therefore, there is no issue of new matter.

The Office Action stated that the Oath/Declaration was defective for the reasons set forth on page 2 of the Office Action. In response, Applicants submit herewith a corrected Oath/Declaration.

The specification was objected to for the reasons set forth on pages 2 and 3 of the Office Action. In response, Applicants submit that the specification has been amended to change the application serial number of the priority provisional application from 60/442,309 to 60/422,309. The recitation of U.S. Provisional Patent Application No. 60/442,309 was a typographical error. The correct priority date was claimed in the application, as filed. Benefit of the correct priority application is claimed in the corrected Oath/Declaration.

Claims 1 to 7, 9, 10, 13, 15, 16, 17, 19 to 22, and 24 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,214,191 to Wiktorowicz et al. (Wiktorowicz) for the reasons set forth on pages 3 to 8 of the Office Action;

Claims 8, 14, 18, and 23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Wiktorowicz in view of U.S. Patent No. 4,959,133 to Adcock for the reasons set forth on pages 8 to 11 of the Office Action; and

Claims 11, 12, 25, and 26 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Wiktorowicz in view of U.S. Patent No. 6,162,602 to Gautsch for the reasons set forth on pages 13 of the Office Action.

In response, Applicants submit that the presently claimed invention is directed to an integrated microfluidic device. As recited in claim 1, as amended, the integrated microfluidic device comprises a sample loading chamber and a fluid reservoir connected by a microfluidic channel. The microfluidic channel comprises an inlet and an outlet. The sample loading chamber is configured for loading a sample of charged molecules into the microfluidic device, is positioned at the inlet of the microfluidic channel, and comprises a first electrode and a second electrode configured to generate a first electric field in the sample loading chamber. When generated, the first electric field is configured to transfer

charged molecules in the sample loading chamber to the inlet of the microfluidic channel. The fluid reservoir is configured for unloading a sample of charged molecules from the microfluidic device, is positioned at the outlet of the microfluidic channel, and comprises a third electrode configured to generate a second electric field with at least the second electrode.

Claim 5, as amended, differs from claim 1 in that claim 5 recites a section of matrix material comprising charged molecules in the sample loading chamber, where the first electric field is configured to electro-elute the charged molecules from the section of matrix material, and to transfer the charged molecules to the inlet of the microfluidic channel

Claim 15, as amended, differs from claims 1 and 5 in that claim 15 recites that the sample chamber is a sample unloading chamber, the sample unloading chamber is configured for unloading a sample of charged molecules from the microfluidic device, and is positioned at the outlet of the microfluidic channel, the first electric field is configured to transfer charged molecules from the outlet of the microfluidic channel into the sample unloading chamber, and the fluid reservoir is positioned at the inlet of the microfluidic channel.

Claim 20, as amended, differs from claim 15 in that claim 20 recites a section of matrix material in the sample unloading chamber, where the first electric field is configured to transfer charged molecules from the outlet of the microfluidic channel into the section of matrix material.

Wiktorowicz discloses methods and apparatus for conducting multidimensional electrophoresis of samples within a single apparatus, such that sample components that have been resolved in a first electrophoretic dimension can be directly electrophoresed in a second dimension that is substantially perpendicular to the first, without needing to move or manipulate the sample between the first and second electrophoretic steps. Wiktorowicz, column 2, line 64, to column 3, line 4.

As illustrated in Figures 3 and 4, the device disclosed by Wiktorowicz has a sample loading port 130, at or through which sample is introduced into the separation cavity, and which provides access to the separation cavity for a first electrode 130a for establishing a voltage potential in the loading port 130 (column 7, lines 40 to 44); channel egress ports 136 and 138, located slightly above a slot 140, where the channel egress ports

are for collecting resolved sample components individually from one or more channels after the second electrophoresis step is complete (column 7, lines 63 to 67); and the slot 140, containing an electrode (column 15, lines 57 and 58). Wiktorowicz does not disclose or suggest an electrode in the channel egress ports 136 and 138, and only discloses a single electrode in the loading port 130.

In addition, Wiktorowicz does not disclose or suggest that any port other than loading port 130 is configured for loading samples in to the disclosed device, or that any port other than channel egress ports 136 and 138 is configured for unloading samples from the disclosed device. In particular, Wiktorowicz does not disclose or suggest unloading samples from the disclosed device through slot 140, and, as discussed below, does not disclose or suggest loading or unloading samples onto or from the disclosed device with the liquid loading region 160. The slot 140 and the liquid loading region 160 are not configured for loading samples into the disclosed device or unloading samples from the disclosed device.

Therefore, Wiktorowicz does not disclose or suggest an integrated microfluidic device, comprising a sample loading chamber, configured for loading a sample of charged molecules into the microfluidic device, and comprising a first electrode and a second electrode, and a fluid reservoir, configured for unloading a sample of charged molecules from the microfluidic device, positioned at the outlet of the microfluidic channel, and comprising a third electrode, as recited in present independent claims 1 and 5.

The loading port 130 disclosed by Wiktorowicz contains only a single electrode, and the channel egress ports 136 and 138 disclosed by Wiktorowicz for collecting or unloading resolved samples do not contain an electrode. Therefore, Wiktorowicz does not disclose or suggest the presently claimed invention, as recited in independent claims 1 and 5 and the claims that depend from those claims.

Wiktorowicz also fails to disclose or suggest an integrated microfluidic device, comprising a sample unloading chamber, configured for unloading a sample of charged molecules from the microfluidic device, positioned at the outlet of the microfluidic channel, and comprising a first electrode and a second electrode, and a fluid reservoir, positioned at the inlet of the microfluidic channel, and comprising third electrode, as recited in present independent claims 15 and 20.

Again, the channel egress ports 136 and 138 disclosed by Wiktorowicz for collecting or unloading resolved samples do not contain an electrode. Therefore, Wiktorowicz does not disclose or suggest the presently claimed invention, as recited in independent claims 15 and 20 and the claims that depend from those claims.

The presently claimed invention is further distinguished from the cited art, as follows: With regard to the introduction of samples into the device disclosed by Wiktorowicz and the liquid loading region 160, disclosed by Wiktorowicz, and identified as a sample chamber in the Office Action, Wiktorowicz clearly discloses that samples are loaded only through sample loading port 130, as discussed above. Wiktorowicz, column 7, lines 40 to 44. Wiktorowicz discloses that the liquid loading region 160 is for conveniently introducing and removing separation media to and from the separation cavity before and after electrophoresis. Wiktorowicz, column 6, lines 61 to 64.

One of ordinary skill in the art, following the disclosure of Wiktorowicz, will understand that the liquid loading region 160 is configured to only receive samples that are introduced into sample loading port 130, and transported through the sample transport channel 180 in the first electrophoresis step. Wiktorowicz, column 7, lines 58 to 62, and Figure 3. The samples are then introduced into the separation channels 170 used in the second electrophoresis step. The liquid loading region 160 is not configured for loading a sample of charged molecules into the microfluidic device, as recited in claims 1 and 5, or for unloading a sample of charged molecules from the microfluidic device, as recited in claims 15 and 20.

With regard to electrodes in ports 132 and 135 and the electrode in slot 140 disclosed by Wiktorowicz, and identified by the Office Action as corresponding to the electrodes in the sample loading chamber, sample unloading chamber, and fluid reservoir of the presently claimed invention, Wiktorowicz discloses that the electrodes in ports 132 and 135 are in or near the liquid loading chamber 160, and the slot 140 is located slightly below the channel egress ports 136 and 138. *See*, Figures 3 and 4 and column 7, lines 63 to 65.

As discussed above, the liquid loading chamber 160 is not configured for loading a sample of charged molecules into the microfluidic device disclosed by Wiktorowicz, or for unloading a sample of charged molecules from the microfluidic device, disclosed by Wiktorowicz, and the slot 140 is not configured for unloading a sample of charged

molecules from the microfluidic device disclosed by Wiktorowicz. Instead, Wiktorowicz discloses that samples are loaded into the device in sample loading port 130, and unloaded from the device through channel egress ports 136 and 138.

Wiktorowicz does not disclose or suggest an integrated microfluidic device, comprising a sample loading chamber, configured for loading a sample of charged molecules into the microfluidic device, and comprising a first electrode and a second electrode, and a fluid reservoir, configured for unloading a sample of charged molecules from the microfluidic device, and comprising a third electrode, as recited in claims 1 and 5.

Wiktorowicz also fails to disclose or suggest an integrated microfluidic device, comprising a sample unloading chamber, configured for unloading a sample of charged molecules from the microfluidic device, and comprising a first electrode and a second electrode, as recited in claims 15 and 20.

With regard to the electric fields generated between electrodes in the device disclosed by Wiktorowicz, Wiktorowicz discloses generating a first electric field between electrodes 130a and 132a in ports 130 and 132, respectively for electrophoresis in the first dimension (column 7, lines 40 to 52, and column 15, lines 38 to 43), turning off the first electric field (column 15, lines 46 and 47), and then generating a second electric field between region 126 towards slot 140 for the second electrophoresis step (column 15, lines 47 to 58, and Figure 3).

Wiktorowicz does not disclose or suggest a first electric field, generated by the first and second electrodes in the sample loading chamber, where, when generated, the first electric field is configured to transfer charged molecules in the sample loading chamber to the inlet of the microfluidic channel, and a second electric field, generated by a third electrode in the fluid reservoir with at least the second electrode, as recited in claims 1 and 5.

Wiktorowicz also fails to disclose or suggest a first electric field, generated by the first and second electrodes in the sample unloading chamber, where, when generated, the first electric field is configured to transfer charged molecules from the outlet of the microfluidic channel into the sample unloading chamber, and a second electric field, generated by a third electrode in the fluid reservoir with at least the second electrode, as recited in claims 15 and 20.

With regard to the matrix material, Wiktorowicz discusses the prior art use of a cross-linked matrix. In particular, at column 2, lines 13 to 27, Wiktorowicz states that the prior art discloses

> Isoelectric focusing (IEF) is an electrophoresis method based on the migration of a molecular species in a pH gradient to its isoelectric point (pI). The pH gradient is established by subjecting an ampholyte solution containing a large number of different-pI species to an electric field, usually in a crosslinked matrix. Analytes added to the equilibrated ampholyte-containing medium will migrate to their isoelectric points along the pH gradient.
>
> For complex samples, multidimensional electrophoresis methods have been employed to better separate species that comigrate when only a single electrophoresis dimension is used. The conventional approach to two dimensional electrophoresis is to perform the first dimension in a rigid, usually crosslinked matrix.

At column 2, lines 51 to 60, Wiktorowicz then discloses

> Accordingly, there is a need for a new multidimensional electrophoresis method that is faster and easier to use, which allows the identification and characterization of hundreds or thousands of components in complex mixtures, and which is highly reproducible. Ideally, the method will employ a single separation apparatus for electrophoresis in both dimensions. The method preferably involves a flowable (liquid-state) separation medium that can be easily replaced with fresh media, so that a single apparatus can be used repetitively for multiple samples.

Finally, with regard to the cross-linked matrix material, at column 17, lines 38 to 45, Wiktorowicz discloses that the apparatus and the method do not require a cross-linked matrix, and the apparatus is easily refilled with the same or different media for separating additional samples.

Therefore, Wiktorowicz discloses that the prior art teaches electrophoresis methods and apparatus based on the migration of a molecular species through a cross-linked matrix. That is not the presently claimed invention. In addition, Wiktorowicz teaches that the method and apparatus disclosed by Wiktorowicz does not require a cross-linked matrix. Instead the apparatus and method disclosed by Wiktorowicz use a single separation apparatus for electrophoresis in both dimensions, using a flowable, liquid-state, separation medium that can be easily replaced with fresh media.

Wiktorowicz does not disclose or suggest a section of matrix material comprising charged molecules in a sample loading or unloading chamber, where an electric field generated by a pair of electrodes in the sample loading or unloading chamber is configured to electro-elute charged molecules from or into the section of matrix material, as presently claimed in claims 5 and 20.

Therefore, Wiktorowicz does not disclose or suggest the presently claimed invention.

Adcock does nothing to overcome the deficiencies of Wiktorowicz. Adcock discloses a means and a method for electroblotting or electroelution, where a field is inverted repeatedly over time, until an electrophoretically separated DNA, RNA, or protein is forced out of a gel and to an appropriate receiver by the net field so produced. Adcock does not disclose or suggest the presently claimed integrated microfluidic device, which comprises the elements discussed above with regard to the disclosure of Wiktorowicz.

Even if the disclosure of Adcock was combined with that of Wiktorowicz, the resulting combinations would not provide the presently claimed invention. Instead, the combination would provide the device disclosed by Wiktorowicz, as discussed above, in which an inverted field was applied to the electrode in each of the chambers. That is not the presently claimed invention. Therefore, Wiktorowicz and Adcock, whether taken alone or in combination do not disclose or suggest the presently claimed invention.

Gautsch does nothing to overcome the deficiencies of Wiktorowicz. Gautsch discloses an apparatus and method for nucleic acid base sequencing in which gel electrophoresis employing agarose or polyacrylamide gels is used to separate fragments. Gautsch does not disclose or suggest the presently claimed integrated microfluidic device, which comprises the elements discussed above with regard to the disclosure of Wiktorowicz.

Even if the disclosure of Gautsch was combined with that of Wiktorowicz, the resulting combination would not provide the presently claimed invention. Instead, the combination would provide the device disclosed by Wiktorowicz, as discussed above, in which an agarose or polyacrylamide gel was in one of the chambers. Therefore, Wiktorowicz and Gautsch, whether taken alone or in combination do not disclose or suggest the presently claimed invention.

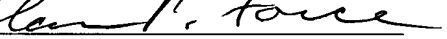
Therefore, as Wiktorowicz, Adcock, and Gautsch, whether taken alone or in combination, do not disclose or suggest the present invention, the present claims are not anticipated by or obvious over those references. Accordingly, it is respectfully requested that the examiner withdraw the rejections of claims 1 to 7, 9, 10, 13, 15 to 17, 19 to 22 and 24 under 35 U.S.C. §102(b) over Wiktorowicz, claims 8, 11, 12, 14, 18, 23, 25 and 26 under 35 U.S.C. §103(a) over Wiktorowicz in view of Adcock, and claims 11, 12, 25 and 26 under 35 U.S.C. §103(a) over Wiktorowicz in view Gautsch.

Applicants thus submit that the entire application is now in condition for allowance, an early notice of which would be appreciated. Should the Examiner not agree with Applicants' position, a personal or telephonic interview is respectfully requested to discuss any remaining issues prior to the issuance of a further Office Action, and to expedite the allowance of the application.

No fee is believed to be due for the filing of this Amendment. Should any fees be due, however, please charge such fees to Deposit Account No. 11-0600.

Respectfully submitted,

KENYON & KENYON LLP

Dated: June 24, 2008 By: 

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